AMENDMENTS TO THE CLAIMS

Claim 1. (original) A method of detecting infectious disease minority variants, comprising:

contacting a nucleic acid sample from a subject or a cell with at least one oligonucleotide pair to form a reaction mixture, wherein a pair comprises a first (P1) and a second (P2) oligonucleotide, wherein P1 comprises a first gene specific region and a first primer region, P2 comprises a second gene specific region and a second primer region; either P1 or P2 comprise a detection region; either P1 or P2 comprise a nucleotide difference in the gene specific region; and P1 and P2 are suitable for ligation to one another;

subjecting the reaction mixture to a ligation reaction; and

amplifying a ligation product to form a reaction product.

Claim 2. (original) The method of claim 1, wherein the minority variant is viral or microbial.

Claim 3. (original) The method of claim 1, wherein the viral minority variant is HIV, HBV, HCV, CMV, influenza, HSV, RSV, or VZV.

Claim 4. (original) The method of claim 3, wherein the viral minority variant is a viral drug-resistant minority variant.

Claim 5. (original) The method of claim 1, wherein the nucleotide difference detected encodes one or more of the amino acid changes K103N, Y181C, K103E, K103R, K103T, G190A, P236L, or another substitution in the viral genome associated with altered susceptibility to one or more antiviral drugs.

Claim 6. (original) A method of differentiating pancreatic cancer from chronic pancreatitis comprising:

contacting a nucleic acid sample from a subject or a cell with at least one oligonucleotide pair to form a reaction mixture, wherein a pair comprises a first (P1) and a second (P2) oligonucleotide, wherein P1 comprises a first gene specific region and a first primer region, P2 comprises a second gene specific region and a second primer region; either P1 or P2 comprise a detection region; either P1 or P2 comprise a nucleotide difference in the gene specific region; and P1 and P2 are suitable for ligation to one another;

subjecting the reaction mixture to a ligation reaction; and

amplifying a ligation product to form a reaction product.

Claim 7. (original) The method of claim 6, wherein the nucleotide difference is in KRAS2.

Claim 8. (original) The method of claim 7, wherein the KRAS2 nucleotide difference is one or more of G35A, G35T, G35C, G34A, G34T, G38A, or A182T.

Claim 9. (original) The method of claim 6, further comprising analyzing the reaction product.

Claim 10. (original) The method of claim 6, further comprising determining the KRAS mutation level.

Claim 11. (original) The method of claim 6, wherein a mutation level of less than about 0.6% indicates chronic pancreatitis.

Claim 12. (original) The method of claim 6, wherein a mutation level of from between about 0.5% to about 80% indicates pancreatic cancer.

Claim 13. (original) The method of claim 6, further comprising monitoring the KRAS mutation levels.

Claim 14. (original) A method of diagnosing a disease in a subject comprising:

obtaining a biological sample from a subject;

contacting the biological sample with at least one oligonucleotide pair to form a reaction mixture, wherein a pair comprises a first (P1) and a second (P2) oligonucleotide, wherein P1 comprises a first gene specific region and a first primer region, P2 comprises a second gene specific region and a second primer region; either P1 or P2 comprise a detection region; either P1 or P2 comprise a nucleotide difference in the gene specific region; and P1 and P2 are suitable for ligation to one another;

subjecting the reaction mixture to a ligation reaction; and

amplifying a ligation product to form a reaction product.

Claim 15. (original) The method of claim 14, wherein the disease is a disease caused by, induced by or related to a nucleotide difference in at least one gene.

Claims 16-22. (cancelled)

Claim 23. (original) A method of forensic identification, comprising:

obtaining a nucleic acid forensic sample;

contacting a nucleic acid forensic sample with at least one oligonucleotide pair to form a reaction mixture, wherein a pair comprises a first (P1) and a second (P2) oligonucleotide, wherein P1 comprises a first gene specific region and a first primer region, P2 comprises a second gene specific region and a second primer region; either P1 or P2 comprise a detection region; either P1 or P2 comprise a nucleotide difference in the gene specific region; and P1 and P2 are suitable for ligation to one another;

subjecting the reaction mixture to a ligation reaction; and

amplifying a ligation product to form a reaction product.

Claims 24-27. (cancelled)

Claim 28. (original) A method of identifying a sample containing an uncommon genetic change, comprising:

obtaining a pooled nucleic acid sample;

contacting the pooled sample with at least one oligonucleotide pair to form a reaction mixture, wherein a pair comprises a first (P1) and a second (P2) oligonucleotide, wherein P1 comprises a first gene specific region and a first primer region, P2 comprises a second gene specific region and a second primer region; either P1 or P2 comprise a detection region; either P1 or P2 comprise a nucleotide difference in the gene specific region; and P1 and P2 are suitable for ligation to one another;

subjecting the reaction mixture to a ligation reaction; and

amplifying a ligation product to form a reaction product.

Claim 29. (original) The method of claim 28, wherein the pooled nucleic acid sample is a pool of samples.

Claim 30. (currently amended) The method of claim 1~~any one of claims 1, 6, 14, 23, or 28~~, wherein the mutated gene specific region is at the 3'end of P1 and/or the 5' end of P2.

Claims 31-39. (cancelled)

Claim 40. (original) A method of detecting a nucleic acid sequence difference, comprising:

contacting a nucleic acid sample with at least one oligonucleotide pair, wherein a pair comprises a first (P1) and a second (P2) oligonucleotide, wherein P1 and P2 bind to a nucleic acid to form a reaction mixture, and wherein P1 comprises a first gene specific region and a first primer binding region and P2 comprises a probe binding region, a second primer binding region and a second gene specific region, wherein there is a gap of one or more nucleotides between the first and second gene specific regions contains the nucleic acid difference;

providing the reaction mixture with a nucleotide complementary to the nucleotide differencenucleic acid difference;

subjecting P1, P2, and the nucleotide to ligation conditions to form a ligation product; and

amplifying the ligation product to form a reaction product.

Claim 41. (currently amended) The method of claim 1~~any one of claims 1, 6, 14, 23, 28 or 40~~, wherein the nucleic acid difference is one or more of KRAS2 nucleotide difference, K103N HIV-1 drug-resistance nucleotide difference, CFTR nucleotide difference, p53 nucleotide difference, or Braf nucleotide difference.

Claim 42. (original) The method of claim 41, wherein the nucleotide ligates to one or more of P1 or P2 if the nucleotide difference is present.

Claims 43-74. (cancelled)

Claim 75. (original) A kit for one of more of detecting infectious disease minority variants, differentiating pancreatic cancer from chromic pancreatitis, diagnosing a disease, forensic identification, comprising:

at least one first (P1) and at least one second (P2) oligonucleotide to form a reaction mixture, wherein P1 comprises a first gene specific region and a first primer region, P2 comprises a second gene specific region and a second primer region; either P1 or P2 comprise a detection region; either P1 or P2 comprise a nucleotide difference in the gene specific region; and P1 and P2 are suitable for ligation to one another; and

instructions for use.

Claim 76. (original) A kit for one of more of detecting infectious disease minority variants, differentiating pancreatic cancer from chromic pancreatitis, diagnosing a disease, forensic identification, or detecting a nucleic acid sequence difference, comprising:

at least one first (P1) and at least one second (P2) oligonucleotide, wherein P1 and P2 bind to a nucleic acid to form a reaction mixture, and wherein P1 comprises a first gene specific region and a first primer binding region and P2 comprises a probe binding region, a second primer binding region and a second gene specific region, wherein there a nucleotide gap between the first and second gene specific regions contains the nucleic acid difference; and

instructions for use.